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Amendment Under 37 C.F.R. § 1.116
Expedited Procedure - Art Unit 1655

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

ASTATKE *et al.*

Appl. No.: 09/608,066

Filed: June 30, 2000

Art Unit: 1655

Examiner: Taylor, J.

Atty. Docket: 0942.4990001/RWE/BJD

For: **Compositions and Methods for Enhanced Sensitivity and Specificity of Nucleic Acid Synthesis**

Amendment and Reply Under 37 C.F.R. § 1.116

Box AF

Commissioner for Patents
Washington, DC 20231

Sir:

In reply to the final Office Action dated October 25, 2001 (Paper No. 13), Applicants submit the following remarks. This Amendment and Reply is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. *See* 37 C.F.R. § 1.121 and MPEP § 714; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this

application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Claims:

Please amend the claims as follows:

Please cancel claims 12-29, 32-34, 60-80 and 83-88 without prejudice to or disclaimer of the subject matter contained therein. Applicants reserve the right to prosecute these claims in one or more continuing or divisional applications.

Remarks

I. Support for Amendments

The foregoing amendments to the claims are sought to place the claims into better to condition for allowance or consideration on appeal, and do not add new matter. Entry and consideration of these amendments are respectfully requested.

II. Status of the Claims

By the foregoing amendments, claims 12-29, 32-34, 60-80 and 83-88 have been cancelled without prejudice or disclaimer. These amendments do not add new matter. Upon entry of the foregoing amendments, claims 81 and 82 are pending in the application, with claim 81 being the sole independent claim.

III. Summary of the Office Action

In the Office Action dated October 25, 2001, the Examiner has made three rejections of the claims. Applicants respectfully offer the following remarks to overcome or traverse each element of this rejection in the Office Action.

IV. The Restriction/Constructive Election

As an initial matter, the Examiner contends that claims 12-29 and 32-34 as amended, and new claims 60-63 and 83-88 are allegedly directed to an invention that is independent from the invention originally claimed (now presented, according to the Examiner, in new

claims 64-80). *See* Paper No. 13 at page 2. The Examiner has therefore withdrawn from consideration claims 12-29, 32-34, 60-63 and 83-88, alleging that a constructive election of the invention of claims 64-82 occurred in Applicants' Reply to Restriction Requirement filed on January 16, 2001. Applicants respectfully disagree. However, to expedite prosecution of the present application, claims 12-29, 32-34, 60-80 and 83-88 have been cancelled without prejudice or disclaimer. As noted above, Applicants reserve the right to prosecute the subject matter of these claims in one or more continuing or divisional applications.

V. The Rejection Under 35 U.S.C. § 102(e) Over Gold Is Traversed

In the Office Action at pages 3-5, the Examiner has rejected claims 64-74 under 35 U.S.C. § 102(e) as being anticipated by Gold *et al.*, U.S. Patent No. 6,020,130 (Doc. "B" cited on the Form PTO-892 attached to the Office Action dated February 14, 2001 (Paper No. 9); hereinafter "Gold"). Applicants respectfully traverse this rejection and contend that Gold does not expressly or inherently disclose the nucleic acid inhibitors of claims 64-74. However, to expedite prosecution and not in acquiescence to this rejection, claims 64-74 have been cancelled. Hence, this rejection has been rendered moot.

VI. The Rejection Under 35 U.S.C. § 103(a) Over Gold Is Traversed

In the Office Action at pages 5-6, the Examiner has rejected claims 80-82 under 35 U.S.C. § 103(a) as being unpatentable over Gold. Applicants respectfully traverse this rejection. However, to expedite prosecution and not in acquiescence to this rejection,

claim 80 has been cancelled thus rendering moot the portion of this rejection that may have applied to claim 80. Applicants offer the following remarks in traversal of this rejection as it may be applied to claims 81 and 82.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). This burden can only be satisfied by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the reference and the knowledge in the art in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Specifically, there must be a reason, suggestion, or motivation in the cited art that would motivate one of ordinary skill to combine the references, and that would also suggest a reasonable likelihood of success in making or using the invention as claimed as a result of that combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). In the present case, this burden has not been satisfied.

As the Examiner has noted, claims 81 and 82 are drawn to methods of producing cDNA molecules from mRNA molecules using one or more reverse transcriptases in the presence of one or more double stranded nucleic acid inhibitors. In contrast, Gold does not expressly or inherently disclose the use of nucleic acid inhibitors in methods of reverse transcription. Indeed, there is no disclosure, suggestion, or contemplation in Gold that the nucleic acid inhibitors disclosed therein could or should be used in conjunction with reverse transcriptases. Instead, as the Examiner has correctly noted, the disclosure of Gold is limited

to methods for the amplification of DNA molecules, particularly via PCR. Thus, Gold is seriously deficient as a primary reference upon which to base a *prima facie* case of obviousness.

Apparently recognizing the deficiencies of Gold, the Examiner attempts to fill these deficiencies by stating that "preparing cDNA from mRNA [is] well known in the art and [is a] standard procedure[] for synthesizing/amplifying nucleic acids." Office Action at page 6, final two lines. However, this statement is irrelevant to the patentability of claims 80 and 81, for at least two reasons.

First, if the use of the methods of Gold in reverse transcription would have been obvious at the time the present invention was made, it is reasonable to expect that such an application would have at least been *suggested* in Gold, which is contemporaneous with the present application. This would particularly be the case if it was true, as the Examiner contends, that reverse transcription for the production of cDNA from mRNA was a "well known component[] of PCR at the time of the invention," Office Action at page 7, lines 1-2, since the development of PCR predates even Gold. However, as noted above, Gold does not disclose, suggest, or even contemplate the use of the methods disclosed therein in reverse transcription. Indeed, Gold does not disclose, suggest or contemplate the use of reverse transcriptase enzymes, nor the use of nucleic acid inhibitors that would bind to reverse transcriptase enzymes. Therefore, far from being obvious, the claimed methods were definitely *non*-obvious to one of ordinary skill reading Gold, even in view of any alleged knowledge of reverse transcription that may have been available in the art.

Second, any alleged knowledge attributed to one of ordinary skill in the art is insufficient to overcome the deficiencies of Gold, because the Examiner has pointed to no actual evidence that would support the notion that one of ordinary skill reading Gold would have been motivated, solely by knowledge allegedly in the art (and which is lacking entirely from Gold), to use the methods of Gold in reverse transcription. As the Federal Circuit has held:

> [r]arely . . . will the skill in the art component operate to supply missing knowledge or prior art to reach an obviousness judgment . . . Skill in the art does not act as a bridge over gaps in substantive presentation of an obviousness case . . . .

Al-Site Corpn. v. VSI International, Inc., 174 F.3d 1308, 1324 (Fed. Cir. 1999). Moreover, an obviousness conclusion must be based on *facts*, rather than on generalities (such as a general and/or unsupported statement of knowledge available in the art). *See In re Warner*, 379 F.2d 1011, 1017 (C.C.P.A. 1967), *cert. denied*, 389 U.S. 1057 (1968); *see also In re Freed*, 425 F.2d 785, 788 (C.C.P.A. 1970).

Hence, Gold does not disclose or suggest the invention as presently claimed, which in itself indicates that the present invention would not have been obvious to the ordinarily skilled artisan. Moreover, the information missing from Gold, which would be required to provide the necessary motivation, has not been shown to have been readily available in the art at the time of filing of the present application. The skilled artisan therefore would not have been motivated to modify the disclosure of Gold in order to make and use the claimed invention. Thus, the burden required to sustain a *prima facie* case of obviousness has not been met.

In view of the foregoing remarks, Applicants respectfully assert that claims 81 and 82 are not rendered obvious by the disclosure of Gold. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are therefore respectfully requested.

VII. The Rejection Under 35 U.S.C. § 103(a) Over Gold In View of Langmore Is Traversed

In the Office Action at pages 7-9, the Examiner has rejected claims 75-79 under 35 U.S.C. § 103(a) as being unpatentable over Gold in view of Langmore *et al.*, U.S. Patent No. 6,117,634 (Doc. "A" on the Form PTO-892 attached to Paper No. 16; hereinafter "Langmore"). Applicants respectfully traverse this rejection and respectfully assert that claims 75-79 are not rendered obvious by the disclosures of Gold and Langmore, alone or in combination. However, to expedite prosecution and not in acquiescence to this rejection, claims 75-79 have been cancelled. Hence, this rejection has been rendered moot.

VIII. Conclusion

All of the stated grounds of rejection have been properly traversed or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all of the outstanding rejections.

It is believed that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt entry and favorable consideration of the foregoing amendments and remarks, and allowance of all pending claims, are earnestly solicited.

Respectfully submitted,

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